

Application No. 09/075,392

Amendment dated February 16, 2005

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (previously presented) An apparatus for performing the polymerase chain reaction in a plurality of liquid reaction mixtures, said apparatus including a plurality of vials containing such liquid reaction mixtures, said vials having an upper portion and a lower portion, said apparatus comprising:
 - an assembly for cycling said vials through a series of temperature excursions;
 - a cover for applying a seating force to said vials and for applying a constant temperature to the upper portion of said vials; and
 - a computing apparatus for controlling said temperature excursions of said assembly and said constant temperature of said cover;said assembly including:
 - a sample block for receiving said vials;
 - a plurality of thermoelectric devices controlled by said computing apparatus;
 - a heat sink;
 - a clamping mechanism positioned so as to clamp said thermoelectric devices between said sample block and heatsink;
 - a heater positioned around the perimeter of said sample block; and
 - a pin having a first end and a second end, said first end in close contact with said sample block and said second end in close contact with said heatsink so as to provide a thermal path between said sample block and said heatsink, said pin being positioned to reduce thermal gradients across said sample block.

Application No. 09/075,392

Amendment dated February 16, 2005

2. (canceled)
3. (previously presented) The apparatus of claim 1 wherein said sample block comprises:
a plurality of sample wells, for receiving sample vials, each well having a top and
bottom;
an upper support plate connecting the tops of said sample wells; and
a bottom plate connecting the bottoms of said sample wells.
4. (original) The apparatus of claim 3 wherein said upper support plate and said sample
wells are electroformed as a single piece.
5. (original) The apparatus of claim 3 wherein said sample block is comprised of silver.
6. (original) The apparatus of claim 3 wherein said sample wells are arranged in an 8 x 12
array.
7. (original) The apparatus of claim 3 wherein said sample block is rectangular.
8. (previously presented) The apparatus of claim 1 wherein said thermoelectric devices
are matched to provide a temperature within 0.2 C for a given input current.
9. (previously presented) The apparatus of claim 1 wherein said thermoelectric devices
comprise:
a first ceramic layer having bonded copper traces;
a second ceramic layer having bonded copper traces, said second ceramic layer
comprising a plurality of ceramic elements; and

Application No. 09/075,392

Amendment dated February 16, 2005

a plurality of bismuth telluride pellets positioned between said first ceramic layer and said second ceramic layer and soldered to said bonded copper traces on said first and second ceramic layers.

10. (original) The apparatus of claim 9 wherein the ceramic of said first and second layer is alumina.

11. (original) the apparatus of claim 9 wherein the ceramic layers have a thickness of 0.508mm.

12. (original) The apparatus of claim 9 wherein said bismuth telluride pellets are soldered using high temperature solder.

13. (previously presented) The apparatus of claim 9 wherein electrical resistance of the devices is determined from the equation:

$$R=nr(h/A)$$

wherein R is the electrical resistance of the device, n is a number equal to how many pellets are in the device, r is resistivity of the bismuth telluride being used in the pellets, h is height of the pellets and A is cross sectional area of the pellets.

14. (previously presented) The apparatus of claim 1 wherein said heatsink comprises:
a plate having a top side and a bottom side;
a plurality of fins extending perpendicularly from said bottom side;
a trench extending around the perimeter of said top side to impede heat loss from said perimeter;
a fan placed in close proximity to said fins to control air flow through said fins; and

Application No. 09/075,392

Amendment dated February 16, 2005

a recess within said plate for receiving a temperature sensor.

15. (previously presented) The apparatus of claim 1 wherein said clamping mechanism comprises:

a spine, said spine having a plurality of openings in said spine for receiving fasteners; and
a plurality of fingers extending laterally from said spine.

16. (previously presented) The apparatus of claim 15 wherein said spine is rectangular in shape.

17. (previously presented) The apparatus of claim 15 wherein said fingers are rectangular in shape.

18. (original) The apparatus of claim 15 wherein said fingers have a top and a bottom and are tapered so as to have less width at said top than at said bottom.

19. (original) The apparatus of claim 15 wherein said fingers have a first end protruding laterally from said spine and a protrusion extending downward from said first end.

20. (original) The apparatus of claim 15 wherein said fingers have a beveled front edge.

21. (original) The apparatus of claim 15 wherein each of said openings are located in close proximity to a corresponding finger.

22. (previously presented) The apparatus of claim 1 wherein said heater comprises an electrically resistive path embedded in a frame shaped film carrier.

Application No. 09/075,392

Amendment dated February 16, 2005

23. (previously presented) The apparatus of claim 22 wherein said electrically resistive path comprises a first set of sections located on opposite sides of said frame shaped carrier having a first power density and a second set of sections located on opposite sides of said frame shaped carrier having a second power density.

24. (previously presented) The apparatus of claim 1 further comprising an associated memory device capable of storing data related to said assembly.

25. (previously presented) The apparatus of claim 1 wherein said cover comprises:
a platen, vertically and horizontally displaceable in relationship to said vials, said platen including:

an array of openings corresponding to locations of said vials, said openings having a perimeter corresponding to a perimeter of said vials;

a skirt extending downward around the perimeter of said platen, said skirt having dimensions corresponding to the perimeter of a standard microtiter tray, said skirt constructed to engage said perimeter of said tray during vertical displacement of said platen, causing said openings in said platen to engage said perimeter of said vials, applying a seating force on said vials for maintaining a snug fit between walls of said sample vials and said assembly for receiving said sample vials;

means for forcibly lowering said platen to maintain said seating force; and

heating means positioned in close contact with said platen to maintain said platen at a constant temperature.

26. (previously presented) The apparatus of claim 1 wherein said assembly comprises at least one device for changing the temperature of said apparatus, further comprising a system for measuring the AC resistance of said thermoelectric device.

Application No. 09/075,392

Amendment dated February 16, 2005

27. (previously presented) The apparatus of claim 26 wherein at least one device has a first heating and cooling surface and a second heating and cooling surface, said system comprising:

a first temperature sensor positioned so as to be in thermal communication with said first heating and cooling surface;

a second temperature sensor positioned so as to be in thermal communication with said second heating and cooling surface;

a bi-polar amplifier circuit for providing power to said thermoelectric device;

a circuit for sensing AC voltage across said thermoelectric device and producing a DC voltage representing said AC voltage;

a circuit for sensing AC current through said thermoelectric device and producing a DC voltage representing said AC current;

a microcontroller programmed to receive said signals from said first and second temperature sensors;

said microcontroller further programmed to cause said bi-polar amplifier to provide power to said thermoelectric device so that said first and second temperature sensor signals indicate equal temperatures;

said microcontroller further programmed to cause an AC voltage to be superimposed on said bi-polar amplifier power;

said microcontroller further programmed to receive said voltages produced by said circuit for sensing AC voltage and from said circuit for sensing AC current;

said microcontroller further programmed to calculate the AC resistance of said thermoelectric device from said voltages;

said microcontroller further programmed to compensate for ambient temperature error by performing a polynomial calculation; and

said microcontroller further programmed to store said compensated AC resistance measurement.

Application No. 09/075,392

Amendment dated February 16, 2005

28. (canceled)

29. (canceled)

30. (canceled)

Application No. 09/075,392

Amendment dated February 16, 2005

31.

(canceled)

Application No. 09/075,392

Amendment dated February 16, 2005

32. (canceled)

33. (previously presented) An assembly for cycling vials of reaction mixtures through a series of temperature excursions, comprising:
a sample block for receiving vials of reaction mixtures;
a plurality of thermoelectric devices;
a heat sink;

Page 17 of 19

Application No. 09/075,392

Amendment dated February 16, 2005

a clamping mechanism positioned so as to clamp said thermoelectric devices between said sample block and said heatsink;

a heater positioned around a perimeter of said sample block;

a pin having a first end and a second end, said first end in close contact with said sample block and said second end in close contact with said heatsink so as to provide a thermal path between said sample block and said heatsink, said pin being positioned to reduce thermal gradients across said sample block; and

means for connecting the assembly to a power source for said heater and a computing apparatus for controlling said temperature excursions of said assembly and said heater.

34.-43. (canceled)

44. (previously presented) The assembly of claim 33, wherein said pin is positioned at the center of the sample block.

45. (previously presented)

The apparatus of claim 1, wherein said pin is positioned at the center of the sample block.